Stereoselective synthesis of mexiletine and structural analogs with chiral tert-butanesulfinamide

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Public Summary:
An asymmetric synthesis of mexiletine and structural analogs was developed using chiral tert-butanesulfinamide to convert precursor ketones to chiral amines. Starting from a-aryloxy ketones, a two-step condensation–reduction procedure provided chiral N-tert-butanesulfinyl amines as immediate precursors to mexiletine or structural analogs. Reduction of the intermediate N-tert-butanesulfinyl imine showed substrate- and reagent-derived stereoselectivity. Following removal of the chiral auxiliary, mexiletine and structural analogs were obtained in high enantiopurity using this approach.

Scientific Abstract:
An asymmetric synthesis of mexiletine and structural analogs was developed using chiral tert-butanesulfinamide to convert precursor ketones to chiral amines. Starting from α-aryloxy ketones, a two-step condensation–reduction procedure provided chiral N-tert-butanesulfinyl amines as immediate precursors to mexiletine or structural analogs. Reduction of the intermediate N-tert-butanesulfinyl imine showed substrate- and reagent-derived stereoselectivity. Following removal of the chiral auxiliary, mexiletine and structural analogs were obtained in high enantiopurity using this approach.